

## **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the applications:

### **Listing of Claims:**

Claims 1-124 (canceled)

125. (currently amended ) A The polynucleotide of claim 204, which comprises two nucleic acid subsequences and which encodes a TNF binding protein,  
wherein the first nucleic acid subsequence encodes a soluble fragment of an insoluble human TNF receptor protein,  
wherein said insoluble human TNF receptor protein has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel,  
and wherein the second nucleic acid subsequence encodes all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region, and  
wherein said TNF binding recombinant protein exhibits specific TNF binding activity.

126. (canceled)

127. (previously presented) The polynucleotide of claim 125 wherein said soluble fragment comprises the amino acid sequence LCAP (SEQ ID NO:12).

128. (previously presented) The polynucleotide of claim 127 wherein said soluble fragment comprises the amino acid sequence VFCT (SEQ ID NO:8).

129. (previously presented) The polynucleotide of claim 128 wherein said soluble fragment comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

130. (previously presented) The polynucleotide of claim 125, 128 or 129 wherein said human immunoglobulin heavy chain is an IgG heavy chain.

131. (canceled)

132. (previously presented) The polynucleotide of claim 130 wherein the human immunoglobulin heavy chain IgG is IgG<sub>1</sub>.

133. (currently amended) A The polynucleotide of claim 204, which comprises two nucleic acid subsequences and which encodes a TNF binding protein,  
wherein the first nucleic acid subsequence hybridizes to the nucleic acid sequence of SEQ ID NO: 3 under conditions that discriminate between the nucleic acid sequence of SEQ ID NO: 3 and the nucleic acid sequence of SEQ ID NO: 1, and  
wherein the first nucleic acid subsequence encodes a soluble fragment of an insoluble human TNF receptor protein,  
wherein said insoluble human TNF receptor protein has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel,  
wherein the second nucleic acid subsequence encodes all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region, and  
wherein said TNF binding recombinant protein exhibits specific TNF binding activity.

134. (previously presented) The polynucleotide of claim 133 wherein the first nucleic acid subsequence is obtainable by a method comprising a step of hybridizing an oligonucleotide probe encoding the peptide of SEQ ID NO: 10 (LPAQVAFXPYAPEPGSTC) to a cDNA library made from HL60 cell extracts.

135. (previously presented) The polynucleotide of claim 133 wherein said soluble fragment comprises the amino acid sequence LCAP (SEQ ID NO 12).

136. (previously presented) The polynucleotide of claim 135 wherein said soluble fragment comprises the amino acid sequence VFCT (SEQ ID NO: 8).

137. (previously presented) The polynucleotide of claim 136 wherein said soluble fragment comprises a nucleic acid sequence encoding the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

138. (previously presented) The polynucleotide of any one of claims 133, 136 or 137 wherein said human immunoglobulin heavy chain is an IgG heavy chain.

139. (canceled)

140. (currently amended) The polynucleotide of claim 138 wherein the human immunoglobulin IgG heavy chain ~~IgG~~ is IgG<sub>1</sub> heavy chain.

141. (currently amended) A The polynucleotide of claim 204, which comprises two nucleic acid subsequences and which encodes a TNF binding protein,

wherein the first nucleic acid subsequence encodes a soluble fragment of an insoluble human TNF receptor protein and comprises a nucleic acid sequence encoding a fragment of SEQ ID NO: 4,

wherein the soluble fragment of SEQ ID NO:4 comprises the amino acid sequence LCAP,

wherein the second nucleic acid subsequence encodes all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region, and

wherein said TNF binding recombinant protein exhibits specific TNF binding activity.

142. (previously presented) The polynucleotide of claim 141 wherein the soluble fragment further comprises the amino acid sequence VFCT (SEQ ID NO: 8).

143. (previously presented) The polynucleotide of claim 142 wherein the soluble fragment further comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

144. (previously presented) The polynucleotide of claim 141 wherein the first nucleic acid subsequence is obtainable by a method comprising a step of hybridizing an oligonucleotide probe encoding the peptide of SEQ ID NO: 10 (LPAQVAFXPYAPEPGSTC) to a cDNA library made from HL60 cell extracts.

145. (previously presented) The polynucleotide of any one of claims 141, 142 or 143 wherein said human immunoglobulin heavy chain is an IgG heavy chain.

146. (canceled)

147. (previously presented) The polynucleotide of claim 145 wherein the human immunoglobulin heavy chain IgG is IgG<sub>1</sub>.

148. (previously presented) The polynucleotide of claim 145 wherein the second nucleic acid subsequence consists essentially of the immunoglobulin-encoding DNA sequence of pCD4Hγ1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-Hγ3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

149. (previously presented) The polynucleotide of claim 148 wherein the second nucleic acid subsequence consists essentially of the immunoglobulin-encoding DNA sequences of pCD4-Hγ1 vector.

Claims 150-154 (canceled)

155. (previously presented) The polynucleotide of claim 125, wherein the TNF binding protein consists of the soluble fragment and all the domains of the constant

region of the human immunoglobulin heavy chain other than the first domain of the constant region.

156. (previously presented) A vector comprising the polynucleotide of claim 125.

157. (previously presented) A host cell comprising the polynucleotide of claim 125.

158. (currently amended) A method of producing a protein, comprising the steps of:

(a) culturing a host cell comprising the polynucleotide of ~~any one~~ of claim 125, and

(b) isolating expressed protein from the cell mass or the culture medium.

159. (previously presented) The method of claim 158 wherein the host cell is a CHO cell.

160. (previously presented) A method of producing a protein, comprising the steps of:

(a) culturing a host cell comprising the polynucleotide of claim 128, and

(b) isolating expressed protein from the cell mass or the culture medium.

161. (previously presented) The method of claim 160 wherein the host cell is a CHO cell.

162. (previously presented) A method of producing a protein, comprising the steps of:

(a) culturing a host cell comprising the polynucleotide of claim 155, and

(b) isolating expressed protein from the cell mass or the culture medium.

163. (previously presented) The method of claim 162 wherein the host cell is a CHO cell.

164. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 132, and
- (b) isolating expressed protein from the cell mass or the culture medium.

165. (previously presented) The method of claim 164 wherein the host cell is a CHO cell.

166. (previously presented) The polynucleotide of claim 133, wherein the TNF binding protein consists of the soluble fragment and all the domains of the constant region of the human immunoglobulin heavy chain other than the first domain of the constant region.

167. (previously presented) A vector comprising the polynucleotide of claim 133.

168. (previously presented) A host cell comprising the polynucleotide of claim 133.

169. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 133, and
- (b) isolating expressed protein from the cell mass or the culture medium.

170. (previously presented) The method of claim 169 wherein the host cell is a CHO cell.

171. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 136, and
- (b) isolating expressed protein from the cell mass or the culture medium.

172. (previously presented) The method of claim 171 wherein the host cell is a CHO cell.

173. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 166, and
- (b) isolating expressed protein from the cell mass or the culture medium.

174. (previously presented) The method of claim 173 wherein the host cell is a CHO cell.

175. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 140, and
- (b) isolating expressed protein from the cell mass or the culture medium.

176. (previously presented) The method of claim 175 wherein the host cell is a CHO cell.

177. (previously presented) The polynucleotide of claim 141, wherein the recombinant protein consists of the soluble fragment and all the domains of the constant region of the human immunoglobulin heavy chain other than the first domain of the constant region.

178. (previously presented) A vector comprising the polynucleotide of claim 141.

179. (previously presented) A host cell comprising the polynucleotide of claim 141.

180. (previously presented) A host cell comprising the polynucleotide of claim 142.

181. (previously presented) A host cell comprising the polynucleotide of claim 143.

182. (previously presented) A host cell comprising the polynucleotide of claim 144.

183. (previously presented) A host cell comprising the polynucleotide of claim 177.

184. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 141, and
- (b) isolating expressed protein from the cell mass or the culture medium.

185. (previously presented) The method of claim 184 wherein the host cell is a CHO cell.

186. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 142, and
- (b) isolating expressed protein from the cell mass or the culture medium.

187. (previously presented) The method of claim 186 wherein the host cell is a CHO cell.

188. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 143, and
- (b) isolating expressed protein from the cell mass or the culture medium.

189. (previously presented) The method of claim 188 wherein the host cell is a CHO cell.



190. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 144, and
- (b) isolating expressed protein from the cell mass or the culture medium.

191. (previously presented) The method of claim 190 wherein the host cell is a CHO cell.

192. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 177, and
- (b) isolating expressed protein from the cell mass or the culture medium.

193. (previously presented) The method of claim 192 wherein the host cell is a CHO cell.

194. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 147, and
- (b) isolating expressed protein from the cell mass or the culture medium.

195. (previously presented) The method of claim 194 wherein the host cell is a CHO cell.

196. (currently amended) A The polynucleotide of claim 204, which encodes a TNF binding protein consisting of

- (a) a soluble fragment of an insoluble human TNF receptor protein, and
- (b) all of the domains of the constant region of a human IgG<sub>1</sub> immunoglobulin heavy chain other than the first domain of said constant region,

wherein said insoluble human TNF receptor protein has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel,

wherein said soluble fragment comprises the amino acid sequences LCAP and VFCT, and

wherein said TNF binding protein exhibits specific TNF binding activity.

197. (previously presented) The polynucleotide of claim 196 wherein the soluble fragment further comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

198. (previously presented) A vector comprising the polynucleotide of claim 196.

199. (previously presented) A host cell comprising the polynucleotide of claim 196.

200. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 196, and
- (b) isolating expressed protein from the cell mass or the culture medium.

201. (previously presented) The method of claim 200 wherein the host cell is a CHO cell.

202. (previously presented) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising the polynucleotide of claim 197, and
- (b) isolating expressed protein from the cell mass or the culture medium.

203. (previously presented) The method of claim 202 wherein the host cell is a CHO cell.

204. (new) A polynucleotide comprising two DNA subsequences, wherein the first subsequence encodes a soluble fragment of an insoluble TNF receptor protein,

wherein said insoluble TNF receptor protein has a apparent molecular weight of either about 55 kilodaltons or about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel, and wherein the second subsequence encodes all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region.

205. (new) The polynucleotide of claim 204 which consists of said first and second subsequences.

206. (new) The polynucleotide of claim 204 or 205, wherein the human immunoglobulin heavy chain is an IgG heavy chain.

207. (new) The polynucleotide of claim 206, wherein the IgG is IgG<sub>1</sub> or IgG<sub>3</sub>.

208. (new) The polynucleotide of claim 207, wherein the IgG is IgG<sub>1</sub>.

209. (new) The polynucleotide of claim 207, wherein the IgG is IgG<sub>3</sub>.

210. (new) A vector comprising the polynucleotide of claim 204 or 205.

211. (new) A host cell comprising the polynucleotide of claim 204 or 205.

212. (new) A method of producing a TNF-binding protein, comprising the steps of:

(a) culturing a CHO cell comprising the polynucleotide of claim 204 or 205,

and

(b) isolating expressed protein from the cell mass or the culture medium.